REMARKS/ARGUMENTS

Status of the Claims

Claims 32, 35 and 36 are allowed.

Claims 1-19, 23-31 and 33 stand rejected.

Claims 13-15, 20-22, 33 and 34 are currently amended.

Claims 1-36 are now pending.

Objection to the Claims

In the Office Action of November 19, 2003, claims 33 and 34 were objected as containing informalities. In response, these claims are currently amended to match the parentheses. Rather than delete the open parenthesis (as suggested in the Office Action), in order to be consistent with the form of the succeeding lines of the claims, these claims have been amended by inserting a closed parenthesis at the end of the lines that were objected to.

Allowed/Allowable Claims

It is gratefully acknowledged that claims 32, 35 and 36 are allowed in the Office Action, and claims 20-22 are indicated as being allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claim 33 is also indicated as being allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. § 112, first paragraph and any objections set forth in the Office Action. Claim 34 is said to be allowable if amended or rewritten to overcome the claim objection set forth in the Office Action. Accordingly, claims 20-22, 33 and 34 are currently amended to fully comply with the stated requirements, and are believed to be ready for allowance.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

Claim 33 stands rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. It is said in the Office Action that there is no original disclosure supporting the upper limit of 25 mole % hydroxy amino acids. Applicant has currently amended claim 33 to correct a typographical error, whereby "25% hydroxy amino acids" is amended to read "15% hydroxy amino acids."

Rejection of Claims Under 35 U.S.C. § 103(a)

Mueller et al.

In the Office Action of November 19, 2003, claims 1-19 and 23-31 are rejected under 35 U.S.C. § 103(a) as being obvious over the article by Mueller et al. *Swiss. Med. Wkly.* 131:23-25 (2001) (*"Mueller et al."*). It is said that the *Mueller et al.* article teaches a bone protein mixture, which includes angiogenic factors such as FGF and TGF-β, in combination with a 5% solution of povidone. The Office deems that sufficient evidence of similarity is present between the *Mueller et al.* article's source of bone proteins and Applicants' claimed mixture of growth factors to shift the burden to Applicants to provide evidence that their claimed mixture of growth factors is unobviously different than the *Muller et al.* article's source of bone proteins.

Submitted herewith in support of this response is the Declaration of Dr. Rama Akella, a named inventor in the instant application, and attached Confidentiality Agreement, which establish that L. K. von Segesser, a named author of the *Mueller et al.* article, obtained the growth factor composition in question from the instant inventors and owner, and carried out the studies reported in *Mueller et al.* in accordance with an agreement between those parties.

Also submitted herewith in support of this response is the Declaration of Richard May, a former officer of the assignee of the instant application, Sulzer Biologics Inc., and a former officer of Sulzer Carbomedics Inc. (a party to the above-mentioned Confidentiality Agreement) during the period of time that is pertinent to the present matter. Mr. May's Declaration establishes that Sulzer Carbomedics Inc. and Sulzer Biologics Inc. were commonly owned at the time of the Confidentiality Agreement and at the time the Mueller et al. article was published.

Applicants submit that the *Mueller et al.* reference is not prior art to the claimed invention. Withdrawal of the *Mueller et al.* article as a 35 U.S.C. § 103 reference against any of the claims herein is respectfully requested.

Chemical Abstract

Claims 1-12 also stand rejected under 35 U.S.C. § 103(a) as being obvious over the *Chemical Abstract* 132:40522x. While acknowledging that the *Chemical Abstract* does not teach a molecular weight or solution concentration for its PVP, the Office Action suggests that it would be obvious to one of ordinary skill in the art at the time Applicants' invention was made, to determine a molecular weight

and solution concentration for the PVP of the *Chemical Abstract* because molecular weight and solution concentration are art-recognized result-effective variables which are routinely determined and optimized in the polymer, solution chemistry, and pharmaceutical arts. In the Office Action of November 19, 2003 it is maintained that

> It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine molecular weight and solution concentration for the PVP of the Chemical Abstract because molecular weight and solution concentration are art-recognized result-effective variables which are routinely determined and optimized in the polymer, solution chemistry, and pharmaceutical arts.

In reply, Applicants respectfully traverse this rejection for at least the reason that the *Chemical Abstract* only contemplates injection of basic fibroblast growth factor, bone morphogenetic protein and PVP to stimulate osteogenesis. By contrast, Applicants' stated PVP molecular weight range of "about 2.5 kD to about 25 kD" relates to compositions for stimulating angiogenesis. Those of skill in the art would recognize that bone growth is quite different than soft tissue growth and/or angiogenesis, and that one could not assume that an optimized parameter for one situation would equally apply in the others. As stated in the instant disclosure, angiogenesis is a complex process involving several different cell types and molecular signaling events. Endothelial cells must secrete proteases to dissolve cell-cell and cell-matrix attachments, migrate and proliferate to form new vascular branches. By contrast, bone growth requires migration, attachment and proliferation of osteogenic precursor cells.

It is implicit in the *Chemical Abstract* that the "result" against which any result-effective parameter would be evaluated is stimulation of osteogenesis -- not angiogenesis. For the sake of argument, even if one were to optimize the PVP molecular weight range for stimulating osteogenesis, there would be no assurance that the resulting molecular weight range would be in the claimed range. There can be no basis, then, for assuming that optimizing a result-effective variable (*i.e.*, PVP molecular weight) for the purposes disclosed in the *Chemical Abstract* would necessarily arrive at the same PVP molecular weight range of Applicants' claimed compositions, or even that such variables are meaningful in the soft tissue context. Clearly there is no teaching or suggestion in the *Chemical Abstract* that would necessarily lead one of ordinary skill in the art to the exact PVP molecular weight range of "about 2.5 kD to about 25 kD," as required in claims 1-12.

The C.C.P.A. has stated, "...[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re*

Aller (220 F.2d 454, 456 (1955). [underlining added] Applicants respectfully submit that in the present case, the general conditions of Applicants' claims, as amended, are not disclosed in the cited reference. For example, PVP molecular weight as a variable parameter, and the requirement for promoting angiogenesis are not disclosed in the *Chemical Abstract*.

The present situation is somewhat analogous to *In Re Antonie*, 559 F.2d 618 (CCPA 1977), in which the court found that recognition of a particular functionality is essential to the obviousness of conducting experiments to determine the value of a particular parameter (tank volume ratio) which will maximize treatment capacity. Also, see *In re Yates*, 663 F.2d 1054, 1056, 211 USPQ 1149, 1151 (CCPA 1981). The determination of a specific parameter can be an obvious expedient only when the art appreciates that the parameter is a result effective variable. In the instant case, the *Chemical Abstract* does not show that the molecular weight range of PVP is a result effective variable with respect to stimulation of osteogenesis, much less having any effect on angiogenesis. Obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established. *In re Rijckaert*, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993). Applicants respectfully submit that no *prima facie* case of obviousness exists with respect to claims 1-12 in view of the *Chemical Abstract*.

Conclusion

Applicants respectfully request reconsideration of this application in light of the foregoing amendments and remarks. In the preceding Remarks/Arguments, Applicants may have at times referred to claim limitations in shorthand fashion, or may have focused on a particular claim element. This discussion should not be interpreted to mean that the other limitations can be ignored or dismissed. The claims must be viewed as a whole, and each limitation of the claims must be considered when determining the patentability of the claims. Moreover, it should be understood that there may be other arguments with respect to patentability which have yet to be raised, but which may be raised in the future. For example, Applicants do not waive the right to show, at their option, an earlier date of invention than discussed herein with respect to any reference, and/or to establish derivation of that reference from a present inventor and/or from the priority document(s). This is believed to be a full complete response to each and every ground of rejection and objection raised in the Office Action of March 26, 2003. If Applicants have incompletely addressed any item, an opportunity to supplement this Response is respectfully requested. The format of this Amendment and Response to Office Action

is believed to conform with the Revised Amendment Practice as described in "Changes To Implement Electronic Maintenance of Official Patent Application Records," 68 Fed. Reg. 38611 (June 30, 2003).

All of the pending claims are believed to be free of the prior art, and reconsideration and withdrawal of the rejections are respectfully requested. If a telephone conference would facilitate the resolution of this matter, the Examiner is invited to telephone the undersigned representative. Should any fees have been inadvertently omitted, or if any additional fees are required or have been overpaid, please appropriately charge or credit those fees to Deposit Account Number 03-2769 of Conley Rose, P.C., Houston, Texas, and consider this a petition for any necessary extension of time.

Respectfully submitted,

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